Conclusion

Therapy is essential in order to prevent graft loss. It is important to be aware that if a patient presents with renal disease recurrence, adequate follow-up is necessary. There were 3.6% and 2.8% respectively per patient year within 5 years. Disease relapse rate and renal disease recurrence rate (four intra- and extrarenal, five focal, one crescentic, four mixed class and one unknown) and three extrarenal relapses (two focal, one crescentic, four mixed class and one unknown). Twenty-two patients had a relapse of disease recurrence (4; 1 focal, one crescentic, two mixed class), infarction (four), acute rejection (four), IFTA (three), sepsis (two), acute rejection (four), crescentic, four mixed class and one unknown. Disease relapse rate and renal disease recurrence rate were 3.6% and 2.8% respectively per patient year within 5 years follow-up. 

Discussion.– This is the largest study to date investigating long-term outcome of renal allografts in AAV. Renal disease recurrence of AAV gave a high-risk for losing the graft within 5 years. It is important to be aware that if a patient presents with renal disease recurrence, adequate therapy is essential in order to prevent graft loss. 

Conclusion.– In a substantial proportion of patients with disease recurrence in the renal allograft (four out of 11) the recurrence led to graft loss within 5 years after transplantation.

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A20 Complement pathways activation in pauci-immune necrotizing glomerulonephritis with ANCA

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Introduction.– Pauci-immune necrotizing glomerulonephritis (PINGN) with anti-neutrophil cytoplasmic autoantibody (ANCA) are observed in systemic vasculitis. Recent studies in murine models indicate that complement is involved in the development of PINGN. We sought to analyse the deposition of complement activation products in kidney biopsies of PINGN, using immunohistochemistry (IHC) and immunofluorescence (IF) staining.

Patients.– Renal biopsies from 11 patients with PR3-ANCA and eight patients with MPO-ANCA were studied with anti-C3d (IHC), anti-C4d (IHC, IF) and anti-C5b-9 (IF) antibodies and compared to C3c deposits observed with standard IF in glomeruli. Control biopsies were two cases of PINGN without C3c deposits, one case of acute post infectious glomerulonephritis (AGN), and one normal kidney biopsy.

Results.– Ten of 11 renal biopsies from patients with PR3-ANCA had a moderate segmental or diffuse granular C3d staining (38.5% of glomeruli), with identical localisation as C3c and C4d deposits. Thus, C4d staining was observed with milder intensity and in only four cases. C5b-9 showed a moderate to intense granular deposit in the floculus and along glomerular basement membrane. The eight renal biopsies from patients with MPO-ANCA had a strong granular C3d staining (57% of glomeruli). As for PR3-ANCA biopsies, C4d was positive only in five of eight renal biopsies. C5b-9 staining was positive in all cases tested, with identical localisation as MPO-ANCA group and in segmental lesions (crescents and necrosis). In control biopsies, C5b-9 was absent in glomerulus floculus of normal kidney but had identical distribution in AGN.

Conclusion.– Complement pathways activation products, including those of the alternative pathway, are detected in the glomeruli of patients with PINGN. We have observed a more intense staining of C3d in patients with MPO-ANCA compared to patients with PR3-ANCA, which may reflect the more chronic/subacute course of MPO-PINGN compared to PR3-PIGN.

Further reading


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A21 Tracheal and bronchial stenoses in granulomatosis with polyangiitis (Wegener) (GPA)

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Background.– Bronchial stenoses (BS) are more uncommon during GPA than subglottic stenoses.
Objective.– To describe refractory BS in a GPA patient.

Case.– In 2008, a 30-year-old man consulting for dyspnea, wheezing, hemoptysis, nasal congestion and epistaxis was diagnosed as having GPA with anti-neutrophil cytoplasm antibodies to proteinase 3, BS, and ear, nose & throat, pulmonary (nodes, alveolar hemorrhage) and renal involvements. Corticosteroids (CS) were combined with IV cyclophosphamide (CYC), IV immunoglobulins (IVIg), mycophenolate mofetil and, finally, azathioprine (AZA). His refractory GPA led to rituximab (RTX) induction therapy (375 mg/m²/week for 4 weeks) in September 2009. He was admitted 2 months later with acute respiratory distress syndrome due to multiple, bilateral BS. Therapeutic bronchoscopy with balloon dilation was successful, and methotrexate (MTX) was added to RTX and AZA. Readmitted for relapsed BS, he received oral CYC induction therapy that achieved remission but BS persisted as sequelae. Maintenance therapy combined AZA and MTX. Follow-up was marked by recurrent, severe, Pseudomonas aeruginosa bronchial pneumonia. In December 2011, despite maintenance therapy (AZA, MTX & CS), he was admitted for a new and severe BS relapse. MTX was stopped; infliximab (5 mg/kg) was started, combined with AZA and CS; this regimen stabilized GPA for 10 months. In October 2012, BS relapsed again, requiring silicone prosthesis insertion. Cytomegalovirus viremia and recurrent, bacterial bronchial pneumonia led to replacing infliximab by IVIg.

Conclusions.– This case illustrates the difficulty of managing GPA-associated BS. Tracheal and endobronchial stenoses must be sought in every GPA patient with a pulmonary abnormality. General and local treatments must be given early because systemic and local management is difficult and ineffective after the inflammatory stage.

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A22

Rituximab therapy for granulomatous polyangiitis (Wegener’s granulomatosis) with refractory granulomatous manifestations

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Introduction.– Granulomatous polyangiitis (GPA) is a potentially fatal granulomatous disease. Cyclophosphamide (CYC) and corticosteroids (CS) remain the preferred treatment for severe GPA, but the in cases with persistent or refractory disease activity treatment remains unclear. Rituximab (RTX) has been reported useful in some cases but data are controversial.

Patients.– Data from five patients with GPA and refractory granulomatous manifestations who received RTX who were reviewed. All patients were PR3-ANCA positive at time of RTX, and in all cases disease activity persisted despite standard treatment with different immunosuppressant drugs (IS) and glucorticoids. Patients had granulomatous manifestations like retro-orbital granuloma (n = 1), lung nodules (n = 1), necrotizing scleritis (n = 1), and subglottic stenosis (n = 2). Clinical characteristics of the patients are summarized in table I. RTX was given intravenously in 2 weekly doses of 1 gm, in combination with other IS. Clinical activity was assessed using BVAS, ANCA serology, and imaging tests.

Results.– RTX was well tolerated. Following RTX, circulating B lymphocytes became undetectable by month 3, and ANCA titers became negative in four patients. Complete clinical remission was achieved in four cases. One patient died due to a bacterial pneumonia and septic shock. GSs were tapered off by 6 to 12 months after RTX infusion. IS therapy was withdrawn in two patients. Two patients experienced a clinical flare after B lymphocyte reconstitution and were successfully retreated with RTX.

Discussion.– There have been few reports of the use of RTX in GPA-patients with refractory granulomatous manifestations. A beneficial response to RTX was seen in four out of five patients with complete remission and PR3-ANCA negativization. RTX was well tolerated, although one patient died due to a severe infection.

Conclusion.– Our results show that RTX therapy can be useful for remission induction in patients with GPA and refractory granulomatous manifestations.

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A23

Upper airway gene expression profiling in granulomatosis with polyangiitis

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Introduction.– Nasal disease occurs in the majority of patients with granulomatosis with polyangiitis (Wegener’s, GPA). We performed whole-genome gene expression profiling of upper airway disease in GPA using a minimally-invasive sampling technique to understand the biology of nasal disease activity in GPA.